

行政院國家科學委員會專題研究計畫成果報告

胃癌BAT-26標記變化的臨床病理意義與核酸誤配修復基因表現 的關係

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中文摘要

具有微衛星體不穩性的腸胃腫瘤是一種有較高突變率的表現型，以往用一個以上的微衛星標記變化加上某些特定基因的突變來決定此種突變表現型的方法耗時且繁雜。最近發現位於 hMSH2 基因 intron 5 上的一段 26 個 deoxyadenosine 標記(簡稱 BAT-26)用於大腸癌的突變表現型決定有很好的敏感性及特異性，是單一可靠的標記。為了探討 BAT-26 的變化是否能作為胃癌突變表現型的標記及具此種變化的腫瘤是否有特殊的臨床病理特徵，吾人收集 119 位胃癌患者的手術檢體，以聚合酵素鏈反應配合電泳分析腫瘤部和非腫瘤部 DNA 在 9 個 dinucleotide 微衛星標記，BAT-26 和 TGF- RII 基因的變化，結果發現具有 BAT-26 變化的胃癌和 TGF- RII 的突變及 3 個以上的微衛星標記不穩定性密切相關，並且這些腫瘤表現特殊的臨床病理特徵，包括位於竇部、腸道型組織型態、進行性胃癌居多、較高的幽門螺旋桿菌感染率、較好的術後存活和較少的淋巴結轉移。這些結果顯示測試 BAT-26 的變化作為一種篩選具特殊亞型、突變表現型及較好預後胃癌的方便且快速方法。

關鍵語：胃癌，突變表現型，微衛星體，BAT-26

Table 1. Correlation of *BAT-26* alterations with replication error (RER) status in 119 patients with gastric cancer

	<i>BAT-26</i> alterations		Total
	Positive (%)	Negative (%)	
RER-negative	0 (0)	87 (100)	87
RER-positive*	17 (53.1)	15 (46.9)	32
at 1 locus	0 (0)	5 (100)	5
at 2 loci	1 (11.1)	8 (88.9)	9
at \geq 3 loci	16 (88.9)	2 (11.1)	18

* at least one of the nine locus was positive

Table 2. The relation of *BAT-26* alterations and clinicopathologic characteristics in 119 patients with gastric cancer

Clinicopathologic characteristics	<i>BAT-26</i> alterations	
	Positive (N=17)	Negative (N=102)
Sex (male/female)	10/7	53/49
Age (mean \pm S.D. in years)	62.5 \pm 16.6	59.4 \pm 14.2
Tumor diameter (cm)	5.1 \pm 2.8	5.3 \pm 2.5
Tumor Stage		
Early	1	20
Advanced	16	82
Tumor location		
Antrum	13**	62
Body and Cardia	4	40
Histologic subtype		
Intestinal	13*	44
Diffuse	4	58
Lymph node metastasis		
Positive	6**	80
Negative	11	22
<i>H. pylori</i> infection		
Positive	16*	64
Negative	1	38
TGF- RII mutations		
Positive	15**	0
Negative	2	102

* p<0.05 and **p<0.01 vs. negative *BAT-26* alterations

Table 3 Proportionate hazards modeling for survival in 119 patients with gastric cancer

Variables	p value
Gender	0.6411
Age	0.0693
Tumor size	0.8699
Histologic subtype	0.3766
T classification	0.0001
N classification	0.0147
M classification	0.0005
<i>BAT-26</i> alteration	0.0001

Fig. 1. Representative examples of *BAT-26* alterations in gastric cancer. Abnormal bands are denoted in lanes 2, 4, 8, 10 with asterisk marks.

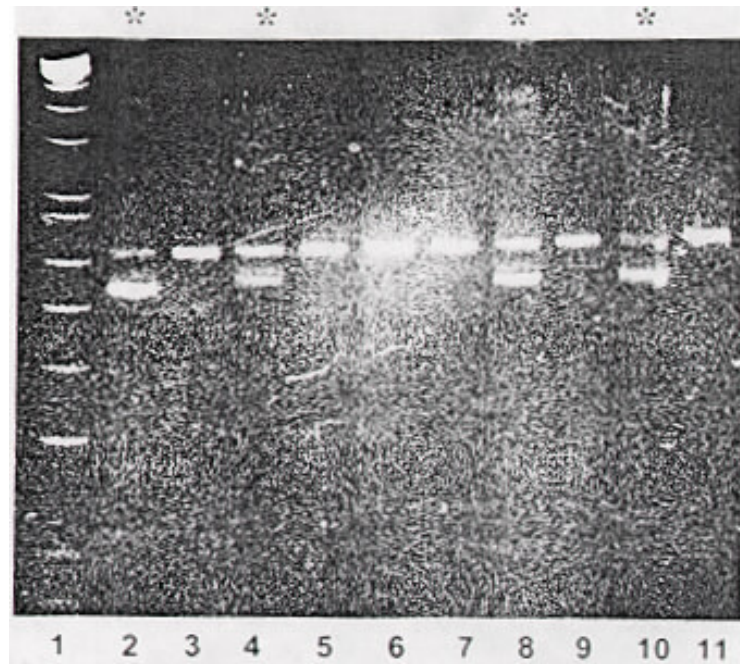
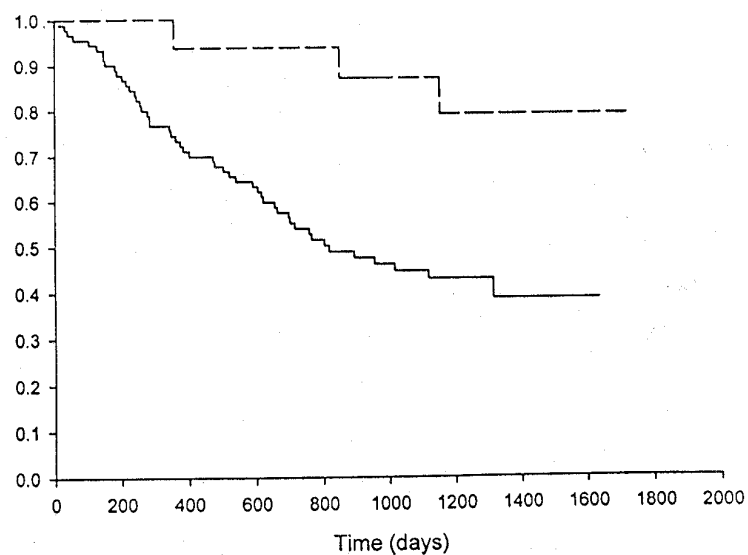


Fig. 2 Kaplan-Meier survival curves of 119 gastric cancer patients stratified by positive (dash line) or negative (solid line) alterations of *BAT-26*.



Abstract

Gastrointestinal tumors with microsatellite instability (MSI) represent a mutator phenotype. It is time-consuming and laborious to determine such a phenotype by the presence of more than one microsatellite alteration together with mutations in some cancer genes that are targets of MSI. BAT-26, a repeat of 26 deoxyadenosine localized in intron 5 of hMSH2 gene, has been reported as a reliable indicator of mutator phenotype in colorectal cancers. To investigate whether BAT-26 is a useful marker for a mutator phenotype with distinct clinicopathologic features in gastric cancer (GC), 119 GC specimens and matched non-tumor tissue were examined by polymerase chain reactions with electrophoresis for 9 dinucleotide microsatellites and BAT-26, and frameshift mutations of transforming growth factor-beta type II receptor (TGF- β RII) gene. GC with BAT-26 alterations was highly correlated with multiple microsatellite alterations (≥ 3 loci) and frameshift mutations of TGF- β RII, and predominantly showed antral location, intestinal histologic subtype, advanced stage, a higher rate of *Helicobacter pylori* infection, a better postoperative survival and less lymph node metastasis. These results show testing of BAT-26 alterations is a convenient and rapid screening method for identifying a subset of GC with a mutator phenotype and better prognosis.

Key Words: Gastric cancer, mutator phenotype, microsatellite, BAT-26

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即將發表之論文

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